JP2003012686

Title:
PYRAZOLE DERIVATIVE

Abstract:

PROBLEM TO BE SOLVED: To provide a pyrazole derivative useful as an agent for the prevention and/or treatment of diabetes or its pharmacologically permissible salt. SOLUTION: The pyrazole derivative is expressed by general formula (I) [R<1> is H, a substituted or unsubstituted lower alkyl or a substituted or unsubstituted lower alkoxy; R<4> is a substituted or unsubstituted lower alkyl or a substituted or unsubstituted lower alkoxy; R<2> is gluconopyranosyl group (the hydroxy group in the gluconopyranosyl group may be protected); and R<3> is a substituted or unsubstituted aryl or a substituted or unsubstituted aromatic heterocyclic group]. The invention further relates to a pharmacologically permissible salt of the derivative.

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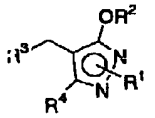
最終頁に続く

(54)【発明の名称】　ピラゾール誘導体

(57)【要約】
【課題】　本発明の目的は、糖尿病予防および／または治療剤として有用なピラゾール誘導体またはその薬理学的に許容される塩を提供することにある。
【解決手段】　一般式（Ｉ）
【化１９】



(I)

［式中、R^1は水素原子、置換もしくは非置換の低級アルキルまたは置換もしくは非置換の低級アルコキシを表し、R^4は置換もしくは非置換の低級アルキルまたは置換もしくは非置換の低級アルコキシを表し、R^2はグルコピラノシル基（グルコピラノシル基中の水酸基は保護されていてもよい）を表し、R^3は置換もしくは非置換のアリールまたは置換もしくは非置換の芳香族複素環基を表す］で表されるピラゾール誘導体またはその薬理学的に許容される塩を提供する。

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:36456 CAPLUS <<LOGINID::20060731>>
DN 138:90016
TI Preparation of 3-pyrazolyl glycosides for treatment of diabetes
IN Shirakura, Shiro; Ito, Yasuhiko; Kusaka, Hiroko; Kusaka, Hideaki; Takeshita, Kenichi; Matsumoto, Yoshiko; Abe, Masayuki; Ota, Yoshihisa; Nomoto, Yuji
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

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PI	JP 2003012686	A2	20030115	JP 2001-200388	20010702 <—
PRAI	JP 2001-200388		20010702		

OS MARPAT 138:90016
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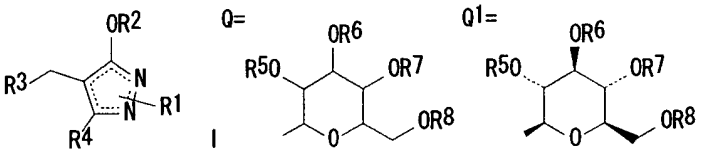

AB 3-Pyrazolyl glycosides, in particular 3-pyrazolyl β-D-glucopyranosides [I; R1 = H, (un)substituted lower alkyl or lower alkoxy; R4 = (un)substituted lower alkyl or lower alkoxy; R5-R8 = H, hydroxy-protecting group; when at least one of R5-R8 is a hydroxy-protecting group and R5-R8 is H and also R1 is (un)substituted lower alkyl or lower alkoxy, R3 is (un)substituted aryl or heterocyclyl; or when R5-R8 is H and R1 is H or lower alkyl, R3 is p-(un)saturated lower alkylsulfonylaryl, or substituted aryl, or (un)substituted aromatic heterocyclyl] or pharmacol. acceptable salts thereof are prepared Also disclosed are preventives or remedies for diabetes or diabetes complications, blood sugar-lowering agents, or Na+-glucose cotransporter (sodium-glucose cotransporter) (SGLT) inhibitors containing the above compds. I as the active ingredients. Thus, to a solution of 4.00 g 1,2-dihydro-4-[(4-methylthiophenyl)methyl]-5-trifluoromethyl-3H-pyrazol-3-one and 14.78 g 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl bromide in 300 mL MeCN was added 9.69 g K2CO3 and stirred at room temperature for 3 days to give 58% 4-[(4-methylthiophenyl)methyl]-3-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)oxy]-5-trifluoromethyl-1H-pyrazole which (908 mg) was stirred with a mixture of 15 mL ethanol and 505 aqueous K2CO3 at room temperature for 1 h to give 7% 4-[(4-methylthiophenyl)methyl]-3-[(β-D-glucopyranosyl)oxy]-5-trifluoromethyl-1H-pyrazole (II). To a solution of 22 mg II in 1 mL MeOH was added 7 mg m-chloroperbenzoic acid and stirred at room temperature for 4 h to give 20% 4-[(4-methylsulfinylphenyl)methyl]-3-[(β-D-glucopyranosyl)oxy]-5-trifluoromethyl-1H-pyrazole (III). In a SGLT inhibition assay, III showed IC50 of 0.0466 μM for inhibiting the uptake of [14C]AMG in proximal tubule epithelial cell lines (LLC-PK1). III at 1 mg/kg i.v. increased the urinary excretion of glucose from 502±61 μg/2 h (control) to 62,077±10,456 μg/2 h in male SLC SD rats.